Cushing disease

Cushing disease is caused by elevated levels of a hormone called cortisol, which leads to a wide variety of signs and symptoms. This condition usually occurs in adults between the ages of 20 and 50; however, children may also be affected. The first sign of this condition is usually weight gain around the trunk and in the face. Affected individuals may get stretch marks (striae) on their thighs and abdomen and bruise easily. Individuals with Cushing disease can develop a hump on their upper back caused by abnormal deposits of fat. People with this condition can have muscle weakness, severe tiredness, and progressively thin and brittle bones that are prone to fracture (osteoporosis). They also have a weakened immune system and are at an increased risk of infections. Cushing disease can cause mood disorders such as anxiety, irritability, and depression. This condition can also affect a person's concentration and memory. People with Cushing disease have an increased chance of developing high blood pressure (hypertension) and diabetes. Women with Cushing disease may experience irregular menstruation and have excessive hair growth (hirsutism) on their face, abdomen, and legs. Men with Cushing disease may have erectile dysfunction. Children with Cushing disease typically experience slow growth.

Frequency

Cushing disease is estimated to occur in 10 to 15 per million people worldwide. For reasons that are unclear, Cushing disease affects females more often than males.

Genetic Changes

The genetic cause of Cushing disease is often unknown. In only a few instances, mutations in certain genes have been found to lead to Cushing disease. These genetic changes are called somatic mutations. They are acquired during a person's lifetime and are present only in certain cells. The genes involved often play a role in regulating the activity of hormones.

Cushing disease is caused by an increase in the hormone cortisol, which helps maintain blood sugar levels, protects the body from stress, and stops (suppresses) inflammation. Cortisol is produced by the adrenal glands, which are small glands located at the top of each kidney. The production of cortisol is triggered by the release of a hormone called adrenocorticotropic hormone (ACTH) from the pituitary gland, located at the base of the brain. The adrenal and pituitary glands are part of the hormone-producing (endocrine) system in the body that regulates development, metabolism, mood, and many other processes.

Cushing disease occurs when a noncancerous (benign) tumor called an adenoma forms in the pituitary gland, causing excessive release of ACTH and, subsequently, elevated production of cortisol. Prolonged exposure to increased cortisol levels results in the signs and symptoms of Cushing disease: changes to the amount and distribution of body fat, decreased muscle mass leading to weakness and reduced stamina, thinning skin causing stretch marks and easy bruising, thinning of the bones resulting in osteoporosis, increased blood pressure, impaired regulation of blood sugar leading to diabetes, a weakened immune system, neurological problems, irregular menstruation in women, and slow growth in children. The overactive adrenal glands that produce cortisol may also produce increased amounts of male sex hormones (androgens), leading to hirsutism in females. The effect of the excess androgens on males is unclear.

Most often, Cushing disease occurs alone, but rarely, it appears as a symptom of genetic syndromes that have pituitary adenomas as a feature, such as multiple endocrine neoplasia type 1 (MEN1) or familial isolated pituitary adenoma (FIPA).

Cushing disease is a subset of a larger condition called Cushing syndrome, which results when cortisol levels are increased by one of a number of possible causes. Sometimes adenomas that occur in organs or tissues other than the pituitary gland, such as adrenal gland adenomas, can also increase cortisol production, causing Cushing syndrome. Certain prescription drugs can result in an increase in cortisol production and lead to Cushing syndrome. Sometimes prolonged periods of stress or depression can cause an increase in cortisol levels; when this occurs, the condition is known as pseudo-Cushing syndrome. Not accounting for increases in cortisol due to prescription drugs, pituitary adenomas cause the vast majority of Cushing syndrome in adults and children.

Inheritance Pattern

Most cases of Cushing disease are sporadic, which means they occur in people with no history of the disorder in their family. Rarely, the condition has been reported to run in families; however, it does not have a clear pattern of inheritance.

The various syndromes that have Cushing disease as a feature can have different inheritance patterns. Most of these disorders are inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Other Names for This Condition

- hypercortisolism
- pituitary ACTH hypersecretion
- pituitary Cushing syndrome
- pituitary-dependant Cushing syndrome

- pituitary-dependant hypercortisolism
- pituitary-dependant hypercortisolism disorder

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Pituitary dependent hypercortisolism
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0221406/

Other Diagnosis and Management Resources

- MedlinePlus Encyclopedia: Cortisol Level
  https://medlineplus.gov/ency/article/003693.htm
- MedlinePlus Encyclopedia: Cushing Disease
  https://medlineplus.gov/ency/article/000348.htm
- The Endocrine Society's Clinical Guidelines: The Diagnosis of Cushing's Syndrome
  https://www.endocrine.org/~/media/endosociety/Files/Publications/Clinical%20Practice%20Guidelines/Cushings_Guideline.pdf

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Cortisol Level
  https://medlineplus.gov/ency/article/003693.htm
- Encyclopedia: Cushing Disease
  https://medlineplus.gov/ency/article/000348.htm
- Health Topic: Cushing's Syndrome
  https://medlineplus.gov/cushingssyndrome.html

Genetic and Rare Diseases Information Center

- Cushing's syndrome
  https://rarediseases.info.nih.gov/diseases/6224/cushings-syndrome

Additional NIH Resources

- Eunice Kennedy Shriver National Institute of Child Health and Human Development
  https://www.nichd.nih.gov/health/topics/cushing/Pages/default.aspx
- National Endocrine and Metabolic Diseases Information Service
  https://www.niddk.nih.gov/health-information/endocrine-diseases/cushings-syndrome
- National Institute of Neurological Disorders and Stroke
  https://www.ninds.nih.gov/Disorders/All-Disorders/Cushings-Syndrome-Information-Page

Educational Resources

- Cleveland Clinic
  http://my.clevelandclinic.org/health/articles/cushings-syndrome
- CLIMB Information Sheet
  http://www.climb.org.uk/IMD/Charlie/CushingSyndrome.pdf
- Disease InfoSearch: Pituitary dependent hypercortisolism
  http://www.diseaseinfosearch.org/Pituitary+dependent+hypercortisolism/9118
- JAMA Patient Page
  http://jamanetwork.com/journals/jama/fullarticle/1104780
- Johns Hopkins Medicine
  http://www.hopkinsmedicine.org/neurology_neurosurgery/centers_clinics/pituitary_center/conditions/cushings-disease.html
- MalaCards: pituitary-dependent cushing's disease
  http://www.malacards.org/card/pituitary_dependent_cushings_disease
- Merck Manual for Patients and Caregivers
  http://www.merckmanuals.com/home/hormonal-and-metabolic-disorders/adrenal-gland-disorders/cushing-syndrome

- Monroe Carell Jr. Children's Hospital at Vanderbilt: Overactive Adrenal Glands/ Cushing's Syndrome in Children
  https://childrenshospital.vanderbilt.org/library/article.php?ContentTypeId=90&ContentId=P01968&Category=SearchTitle&section=33153&term=d&
- Orphanet: Cushing disease
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=96253

Patient Support and Advocacy Resources

- CLIMB: Children Living with Inherited Metabolic Diseases
  http://www.climb.org.uk/
- Cushing's Support & Research Foundation
  https://csrf.net/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/cushing-syndrome/
- Pituitary Network Association
  https://pituitary.org/knowledge-base/disorders/cushing-s-syndrome
- The MAGIC Foundation
  https://www.magicfoundation.org/Growth-Disorders/Cushing-Syndrome/

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Cushing+disease%22+OR+%22Hypercortisolism%22+OR+%22Cushing+Syndrome%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Cushing+disease%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- PITUITARY ADENOMA, ACTH-SECRETING
  http://omim.org/entry/219090

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